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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/677,653	10/03/2000	Peter Daniel Christian	A-58631-4/RFT/DJM	7496

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EXAMINER	
LUCAS, ZACHARIAH	
ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 10/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/677,653	CHRISTIAN ET AL.	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15-23 and 33-41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-23 and 33-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. Currently, claims 15-23, and 33-41 are pending in the present application. Claims 15-23 were rejected, and claim 24 was withdrawn as to a non-elected invention in the prior action, mailed on January 15, 2004. In the response, filed on July 15, 2004, the Applicant amended claim 15, cancelled claim 24, and added new claims 33-41.

2. This action is being made Non-Final because it raises new grounds of rejection not made in the prior action, and not necessitated by amendment.

Specification

3. **(New Objection)** The disclosure is objected to because of the following informalities: the Applicant is requested to resubmit copies of originally filed pages 41, 89, 102, 103, 107, and 113 as originally filed in the present application which appear to be missing from the PTO application file.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. **(New Rejection)** Claims 18 and 36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims read on the claimed nucleic acids wherein "the capsid protein is HaSV P71 (SEQ ID NO: 50)." It is not clear from the claim language whether the sequence identified in the parenthetical statement is intended to be a claim limitation (i.e. if the claim is limited to the HaSV P71 of SEQ ID NO: 50), or if the sequence is intended as merely an example of such sequences. Clarification is required.

6. **(New Rejection)** Claims 15, 16, 19-23, 33, 34, and 37-41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims read on nucleic acids encoding, in part, capsid proteins of an "insect small RNA virus." However, it is not clear what viruses the Applicant considers to fall within the scope of such viruses. In particular, the Applicant indicates that certain art references teach that these viruses include any insect RNA virus of less than 40nm, while another teaches that they include viruses of 40nm of less, and a third reference by one of the present inventors includes in the term one of only three groups of viruses. Page 2. In view of these multiple and inconsistent definitions of the term, it is unclear what the Applicant considers to fall within the scope of an "insect small RNA virus."

Clarification is required.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

> pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. **(Prior Rejection- Maintained)** Claims 15-19, 21, and 22 were rejected in the prior action under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The rejection is withdrawn from claim19 because the claim refers only to insecticidal toxins, which were identified in claim 15 as proteinaceous in nature. The rejection is extended to new claims 33-36, and 39, and 40.

The Applicant traverses the rejection on the grounds that the claims are directed to delivery vehicle, and not to the compounds being delivered. The Applicant also notes support in the application and art teaching effective anti-insect toxins. However, none of the teachings in the application or the art provide any examples or guidance towards specific nucleotide sequences that are themselves insecticidal.

The following quotation from section 2163 of the Manual of Patent Examination Procedure is a brief discussion of what is required in a specification to satisfy the 35 U.S.C. 112 written description requirement for a generic claim covering several distinct inventions:

> The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice..., reduction to drawings..., or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus... See Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406.
>
> A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

Thus, when a claim covers a genus of inventions, the specification must provide written description support for the entire scope of the genus. Support for a genus is generally found where the applicant has provided a number of examples sufficient so that one in the art would recognize from the specification the scope of what is being claimed, or where the application identifies a particular function that correlates with a known or disclosed structure.

As indicated above, and in the prior actions, the Applicant has provided neither form of support for the claims as they are drawn to insecticidal nucleic acid sequences. The Applicant's arguments that the claims are directed to a delivery mechanism are not persuasive because the description of the first part of the claimed sequences (the viral capsid protein encoding sequence) provides no information as to the sequence of the toxic portion of the nucleic acid.

The Applicant has also noted claims in other issued patents (to other inventors) drawn broadly to vectors useful for the delivery of nucleic acids to target cells. Applicant argues that these patents demonstrate an analysis of the claimed compositions based on the use of the compositions for the delivery of agents in general, and not on specific agents. This argument is not found persuasive for two reasons. First, the allowability of claims in separate applications is determined based on facts unique to each applications. Examples of such unique facts are the filing date of the application (determining the date at which the knowledge in the art is considered), the teachings in the applications, and the inventions being claimed. In view of these unique factors, the fact that a set of claims was found allowable to one applicant does not demonstrate that the same claims would be allowable if presented in a separate application by a different applicant.

This argument is also not found persuasive because the present claims are rejected based on language in the claims directed to the delivery of a specific category of nucleic acids, and not to the delivery of nucleic acids or bioactive agents in general, as the Applicant asserts is the case in the cited patents. Because the Applicant has claimed compositions for the delivery of this category of nucleic acids, the Applicant must provide descriptive support for this group. None of these patents provide any indication that the rejected categories of compositions (the genera of insecticidal ribozymes and antisense nucleic acids) were recognized in the art. Nor is there any indication that this category of inventions was even made of issue during the examination of the patent applications from which they were issued. Because the patents provide no basis for assuming a class of insecticidal nucleic acids was specifically made of issue in those patents, it is not clear how the generic claims that were found allowable in the cited patents provide evidence of the allowability of the currently rejected genus. In the absence of some nexus between the claims of the patents and the rejection of the present application, the Applicant's argument that broad claims in allowed patents demonstrates the allowability of a specific genus not mentioned in those patents is not found persuasive.

For these reasons, and the reasons of record, the rejection is maintained.

9. **(Prior Rejection- Maintained)** Claims 15-19, and 21-23.were rejected in the prior action under 35 U.S.C. 112, first paragraph, because the specification while being enabling for isolated nucleic acids comprising the a first sequence encoding an insect RNA virus capsid protein and a second sequence that encodes an insecticidal protein, does not reasonably provide enablement for the claimed nucleic acids where the second sequence is a ribozyme, antisense, or other

insecticidal nucleic acid sequence. The rejection is withdrawn from claims 19 and 23 because these claims refer only to insecticidal toxins, which were identified in claim 15 as proteinaceous in nature. The rejection is extended to new claims 33-36, and 39, and 40 for the reasons of record.

The Applicant traverses the rejection on the grounds that "the exact identity of the second sequence is not necessary for the practice of the invention," and that its identity need not be determined "until the invention is used by one of skill in the art for a particular application of insecticidal nucleic acid." The Applicant asserts that the test for enablement does not require the teaching of that which is well known in the art. While the Examiner agrees with the Applicant's statement regarding the teaching of what is known in the art, the argument is not found persuasive as the Applicant has presented no evidence that insecticidal nucleic acids, or insecticidal antisense sequences or ribozymes are known in the art. As was indicated in the prior actions, the application provides no examples or guidance to such insecticidal nucleic acid sequences. Nor do such sequences appear to be taught in the art.

Because neither the application nor the art appears to provide an enabling disclosure for insecticidal nucleic acid sequences, those in the art would not be able to make and use the claimed inventions to the extent that they involve such sequences. The rejection is therefore maintained for the reasons above, and the reasons of record.

10. **(New Rejection)** Claims 15-17, and 19-23 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably

convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims read on nucleic acids comprising a sequence encoding an insect small RNA virus capsid protein, wherein the capsid protein comprises an insect midgut cell-binding domain.

The following quotation from section 2163 of the Manual of Patent Examination Procedure is a brief discussion of what is required in a specification to satisfy the 35 U.S.C. 112 written description requirement for a generic claim covering several distinct inventions:

> The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice..., reduction to drawings..., or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus... See Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406.
>
> A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

Thus, when a claim covers a genus of inventions, the specification must provide written description support for the entire scope of the genus. Support for a genus is generally found where the applicant has provided a number of examples sufficient so that one in the art would recognize from the specification the scope of what is being claimed.

The claims of the present application are rejected because the Applicant has not provided sufficient written description support for any nucleic acid encoding an insect small RNA virus capsid protein wherein the capsid comprises a midgut cell binding domain. The current application provides only a single example of a small insect virus capsid that is useful in the claimed inventions (the HaSV P71 protein). Within this protein, the Applicant has identified a region of over 150 amino acids that is responsible for the virus' ability to bind a host cell. Page

112. Thus, the Applicant has identified only one example of a capsid protein binding to a midgut cell, and has provided little information as to what specific structural characteristics of that protein enable midgut cell binding.

While the application additionally provides teachings regarding what other viruses are considered to be insect small RNA viruses (pages 1-3), it does not teach the cell targets of these viruses, or which of these other viruses are able to bind to insect midgut cells. The art, however, teaches that small insect RNA viruses may be found in multiple regions of the insect physiology, and indicates that such viruses are capable of infecting cells in such different regions. See e.g., Scotti et al., Adv Virus Res 26: 117-43 (esp., page 118 and 129). Further, while the art teaches the cloning of genes for certain capsid proteins of other small insect RNA viruses, it is not clear that those in the art would have been aware of which specific viruses were capable of infecting the midgut. See e.g. Agrawal et al., Virology 190: 306-14 (of record in the January 2001 IDS, which both teaches that several members of the Tetraviridae family have been observed to replicate in the midgut, but fails to identify the primary target of the specific virus sequenced in the reference). Although later art teaches that the members of Tetraviridae tend to bind to the midgut, the art also indicates that such is not the case for all insect small RNA virus. Bawden et al., J. Invertebr Pathol 74: 156-63, at page 162 (of record in the January 2001 IDS). Further, as indicated by Bawden (on page 161, right column), it is understood in the art that viral binding to cells is mediated by receptors on the cell surface. However, as was also indicated by Bawden, different viruses target different receptors. It is also known in the art that there are many different receptors present on each cell. Thus, the disclosure of one viral capsid that targets one (unknown) cell receptor on a midgut cell does not provide sufficient information such that those

in the art would be able to identify from that disclosure other viruses, and their capsid protein, with tropism towards midgut cells.

Because neither the application, nor the art identifies specific virus capsids, or provides any other means of identifying such capsid other than by function, the Applicant has not provided adequate written description support for the full scope of the claimed compositions.

11. **(New Rejection-Necessitated by Amendment)** Claims 15-17, and 19-23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the claimed nucleic acids wherein which encode insect small RNA virus capsid proteins, does not reasonably provide enablement for the claimed compositions wherein the nucleic acids encode any capsid protein comprising a midgut cell binding domain.

In making a determination as to whether an application has met the requirements for enablement under 35 U.S.C. 112 ¶ 1, the courts have put forth a series of factors. See, In re Wands, 8 USPQ2d 1400, at 1404 (CAFC 1988); and Ex Parte Forman, 230 U.S.P.Q. 546 (BPAI 1986). The factors that may be considered include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. Id. While it is not essential that every factor be examined in detail, those factors deemed most relevant should be considered.

The claims have been described above. As was also described above, the application provides only a single working example of an insect small RNA virus capsid protein comprising

an insect midgut binding protein (the p71 protein). While the application suggests a potential cellular binding site in this protein, the application does not appear to identify a specific sequence of residues that correlates with a binding site in the protein. Nor does that application provide any guidance towards other proteins with such a binding domain, or provide any structural feature of such proteins that correlate with a midgut binding function.

The art teaches both that insect small RNA virus are ubiquitous in nature, have a broad host range, and may infect cells in multiple regions of insect physiology. Scotti et al., Adv Virus Res 26: 117-43 (esp., page 118 and 129). Further, while the art recognizes that several small insect viruses do replicate in midgut cells, the art at the time of the filing date indicates that little was known about the actual replicative cycle of individual viruses. Agrawal et al., Virology 306-314, page 306, right column, second paragraph. Other references also note that, while certain viruses were known to generally target midgut cells, such was not the case with all insect small RNA viruses. See e.g., Bawden, supra. Before those in the art could make the claimed polynucleotides, those in the art would first have to identify other viruses with midgut binding ability, and identify which proteins of the virus are able to bind such cells.

In view of the teachings in the art regarding the scope of cells and receptors targeted by the viruses, the limited teachings in the art leading them to specific viruses binding midgut cells, and the lack of any means by which to structurally identify other capsid proteins that bind midgut cells, the Applicant has not provided sufficient information such that those in the art would be able to practice the full scope of the claimed invention without undue experimentation.

12. **(New Rejection-Necessitated by Amendment)** Claims 33-41 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. These claims read on the nucleic acids as described above, wherein the "capsid protein protects said second sequence from degradation." The claims are rejected because the Applicant has not demonstrated that a capsid protein alone is capable of inhibiting degradation of the RNA sequences. Rather, the only description in the application of the protection of RNA from degradation is through the use of whole capsovectors- each comprising many copies of the capsid protein. See, page 112. Thus, the Applicant has not enabled the practice of the claimed invention wherein the capsid protein alone, as opposed to a capsovector comprising such proteins, is able to perform the indicated protective function.

It is suggested that the claims be amended to require that the first sequence encodes a capsid protein capable of forming into a capsovector encapsulating the isolated RNA sequence. Because the claims read on embodiments wherein the capsid protein itself, rather than a capsovector comprising such proteins, protects the RNA, the claims are rejected as exceeding the scope of enablement.

13. **(New Rejection-Necessitated by Amendment)** Claims 33, and 35-41 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for embodiments of the claimed nucleic acids the nucleic acid encodes capsid proteins from an insect small RNA virus that, when expressed, protects encapsulated RNA from degradation, does not reasonably

provide enablement for the claimed compositions wherein capsid proteins protect any form of nucleic acid. For the purposes of this rejection, it is assumed that the claims are drawn to nucleic acids encoding a TNA virus capsid capable of forming a capsovector

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. As was indicated above, the Applicant has disclosed the protective capabilities of the capsid proteins only in the form of capsovectors on page 112 of the application. It is noted that this description indicates that the protective capability is dependant on the encapsulation of the RNA to be protects, and teaches only the encapsulation of RNA in the described structures. Id., lines 8-10. See also, pages 82-90, 108-109, and 112 (describing examples of RNA encapsulation by insect small RNA viruses and capsovectors). There is no description in the application, or other indication, that other forms of nucleic acid, such as DNA, would be encapsulated by capsovectors formed of the RNA virus capsid proteins. Furthermore, it recognized in the art that RNA viruses do not comprise DNA. In view of this, those in the art would have had no reasonable expectation of success in the encapsulation of a DNA molecule in an RNA virus capsovector. Thus, without additional teachings indicating how those in the art would be able to encapsulate DNA into the RNA capsovectors, the application has not provided an enabling disclosure for such embodiments of the claimed invention.

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

15. **(Prior Rejection- Withdrawn)** Claims 15, 16, and 19-23 were rejected in the prior action under 35 U.S.C. 103(a) as being unpatentable over Wilcox (U.S. Patent in view of Harley et al. (Virology 69:323-326). It is noted that, although not argued by Applicant, the viruses described in the Harley reference do not appear to be insect small RNA viruses as described in the claims. See e.g., application, pages 1-3, esp. page 2, lines 9-18 (indicating that small RNA insect viruses are those of less than 40 nm in diameter), and page 3, lines 2-6 (indicating that the CPV RNA virus of Harley does not fall within the scope of the small insect RNA viruses). In view of this, the rejection is withdrawn.

Conclusion

16. No claims are allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 571-272-0905. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Z. Lucas
Patent Examiner

James C. Housel 10/1/04

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